Basic Circuit Theory & Patch-clamp Amplifier

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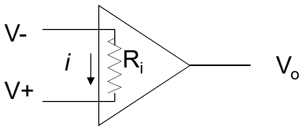
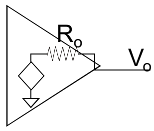
이석호

OP amplifer

The Golden rule of Operational Amplifier (Analog Devices, USA)





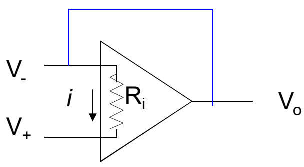
high input resistance ($R_i \rightarrow \infty$)

(*i* between + and – is zero, cf. $R_o \rightarrow 0$)

(-): inverting input

(+): non-inverting input

$V_O = A\,(V_+ - V_-)$



$V_O = A\,(V_+ - V_-)$

If negative feedback line (blue) is connected

$V_- = V_+$, when open loop gain (A) is large ($A > 10^5$)

• *If* $V_- = V_o$,

$$V_o = V_+ A / (1+A) \cong V_+ = V_-$$

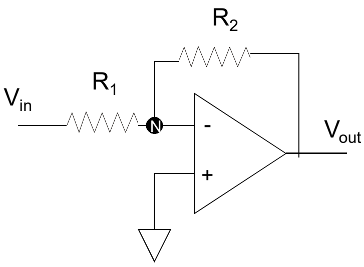
•*Even if* $V_o = x\,V_-$ (by inserting resistor on blue), *as long as* $x \ll A$,

$$x\,V_- = A\,(V_+ - V_-)$$

$$V_- = A / (x + A)\,V_+ \cong V_+.$$

$$\therefore V_+ = V_-.$$

Inverting Amplifier

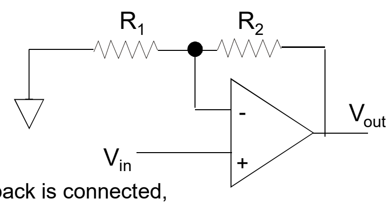


When V_+ is grounded and the negative feedback is connected,
the node between Vo and V- ('N') becomes an **imaginary ground**.

1) **$V_- = V_+ = 0$**
2) **$(V_{in} - V_-) / R_1 + (V_{out} - V_-) / R_2 = 0$** (Kirchhoff`s rule)

$\Rightarrow V_{out} / V_{in} = -R_2 / R_1$.

Non-inverting Amplifier

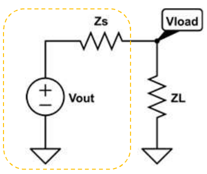


When V_+ is grounded and the negative feedback is connected,
the node between Vo and V- ('N') becomes an **imaginary ground**.

1) **$V_- = V_+ = V_{in}$.**
2) **$(0 - V_{in}) / R_1 + (V_{out} - V_{in}) / R_2 = 0$** (Kirchhoff`s rule)

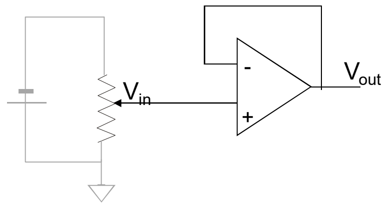
$\Rightarrow V_{out} / V_{in} = 1 + (R_2 / R_1)$.

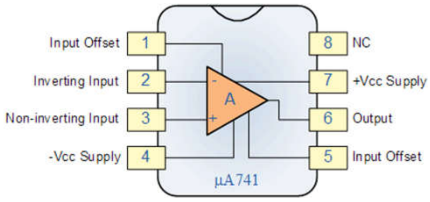
Voltage follower



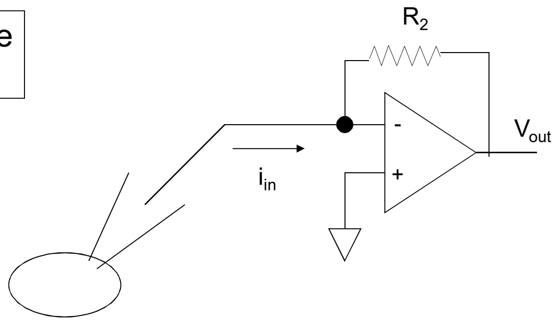
$V_{load} = V_o * (Z_L / Z_L + Z_s)$
As $Z_L \rightarrow 0$, $V_{load} \rightarrow 0$

<u>Ideal Amp.</u> : $Z_s \rightarrow 0$





Current-to-voltage Converter

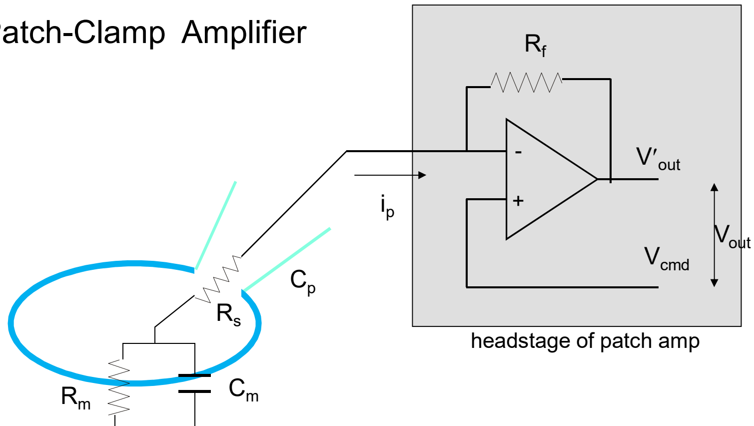


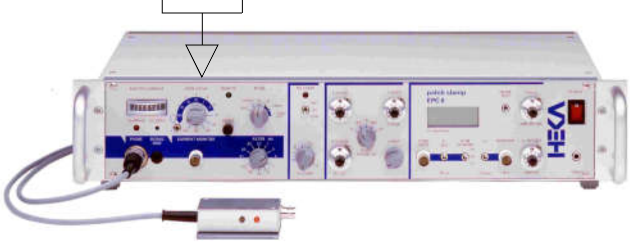
The same circuit as the inverting amplifier except **R1 = 0**,

1) $V_- = V_+ = 0$
2) $i_{in} + (V_{out} - V_-) / R_2 = 0$ (Kirchhoff`s rule)

$\Rightarrow V_{out} = -R_2 \cdot I_{in}$.

Patch-Clamp Amplifier



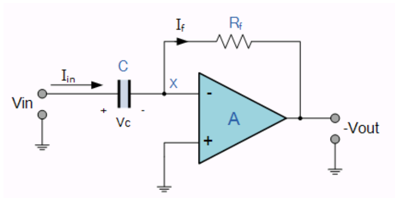


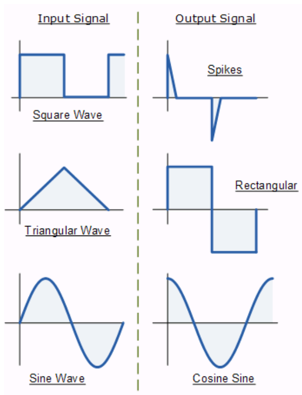
$V_- = V_+ = V_{cmd}$

$i_p + (V'_o - V_{cmd}) / R_f = 0$

$V_{out} = (V'_{out} - V_{cmd}) = - R_f \, i_p$

Differentiator



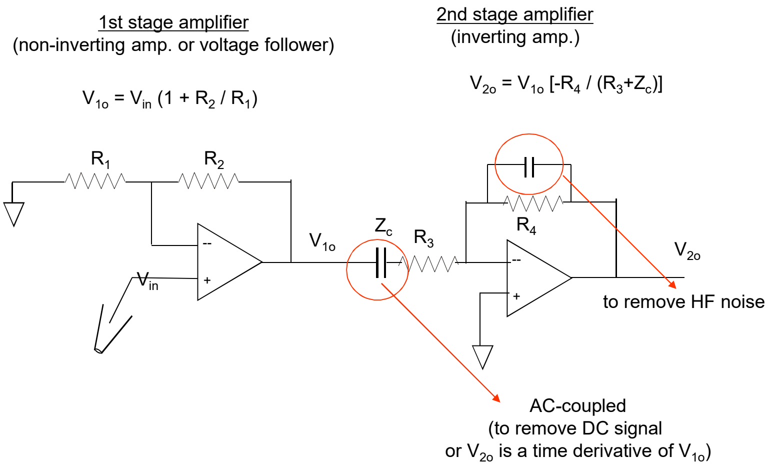


1) $V_- = V_+ = 0$

2) $C\, dV_{in}/dt + V_{out} / R_f = 0$ (Kirchhoff`s rule)

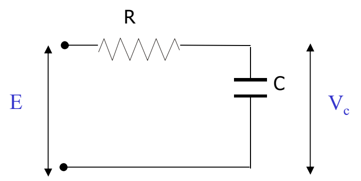
$\Rightarrow V_{out} = -R_f\, C \cdot dV_{in}/dt$

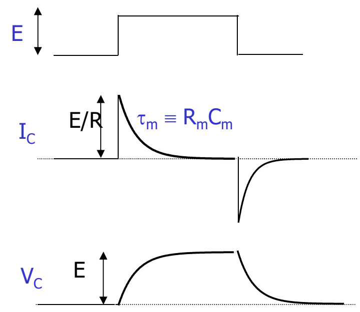
Field potential measurement circuit



RC circuit & patch-clamp signals

RC-Circuit I





$E = V_R + V_C$.

Since $Q = C\,V_C$,

$i_C = dQ/dt = C\,dV_C/dt$

Since $i_R = i_C$,

$(E\text{-}V_C)/R = C \cdot dV_C/dt$

$dV_C/dt + V_C/\tau = E/\tau$, $(\tau \equiv RC)$

$V_C = E\,(1\text{- }\exp(\text{-}t/\tau))$

$I_C = C\,dV_C/dt = (E/R) \cdot \exp(\text{-}t/\tau)$

Solving ODE

- Separate variables

$dv/dt = (1/\tau)(E - v)$

$dv = (1/\tau)(E - v)\,dt$

$dv/(v - E) = -dt/\tau$

$\ln(v - E) = -t/\tau + C$

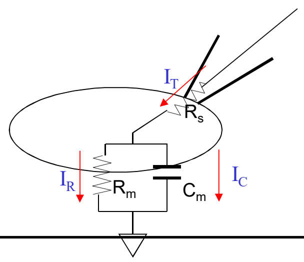
$v(t) - E = A\exp(-t/\tau)$

- Determine constants

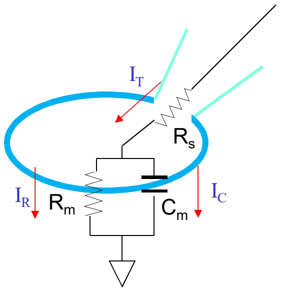
Let $v(0) = v_0 = 0$.

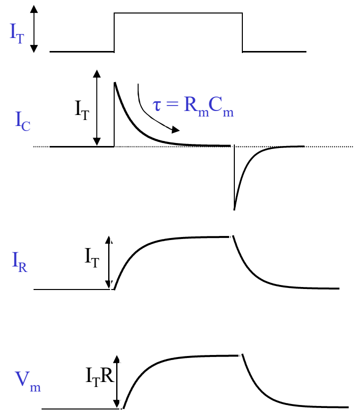
$(v_0 - E) = A$

$v(t) = E\,[1 - \exp(-t/\tau)]$



V_m change to current injection





Voltage change upon current injection

$V_R = I\,R$

$V_C = Q/C_m = \int I_C\,dt / C_m.$

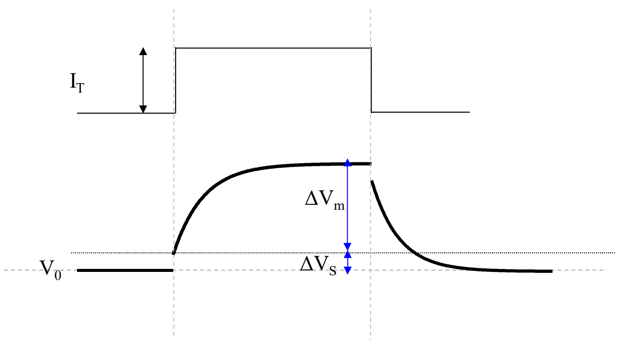
$I_T = I_R + I_C.$

$I_C = I_T \cdot [\exp(-t/\tau)]$

$I_R = I_T - I_C = I_T \cdot [1 - \exp(-t/\tau)],\ \tau \equiv R_mC_m$

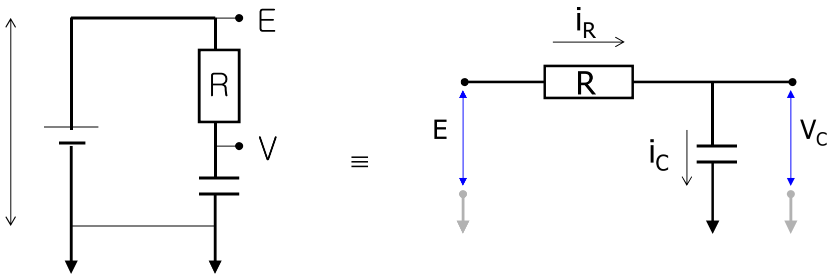
$V_m = V_R = V_C = I_R \cdot R_m = -I_T \cdot R_m \cdot [1 - \exp(-t/\tau)]$

Input Resistance (R_m) = ($\Delta V_{ss} / I_T$) - R_s

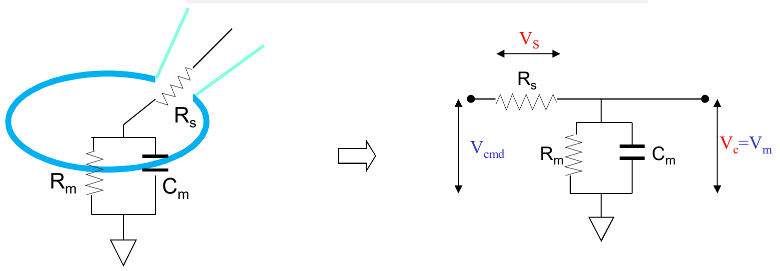


$\Delta E_{ss} = \Delta V_m + \Delta V_S = i_T \cdot (R_m + R_S)$

$E(t) = \Delta V_m \cdot (1 - \exp(-t/\tau_m)) + i_T \cdot R_S$



I_m change to voltage clamp (1)



$V_{cmd} = V_S + V_C$, $I_T = I_m = I_R + I_C$.

$V_{cmd} = I_T \cdot R_S + V_C$.

$= (I_R + I_C) \cdot R_S + V_C$

$= (V_C/R_m + C_m\, dV_C/dt) \cdot R_s + V_C$

$dV_C/dt + V_C/\tau_P = V_{cmd}/\tau_S$,

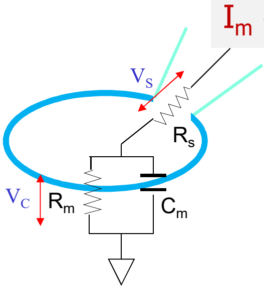
where $\tau_P \equiv R_P C_m$, $\tau_s \equiv R_s C_m$, and $R_P = R_s \cdot R_m / (R_s+R_m)$.

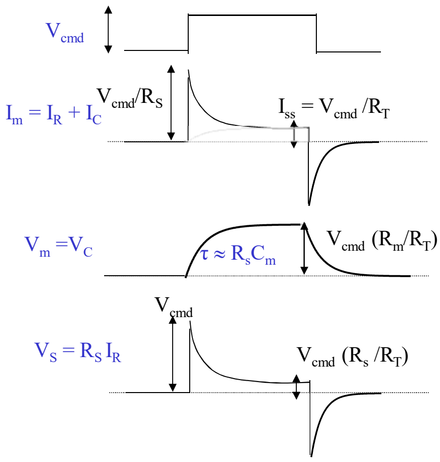
$V_C = V_{cmd} \cdot [R_m/(R_s+R_m)]\, [1 - \exp(-t/\tau_P)]$

$I_C = C_m \cdot dV_C/dt = (V_{cmd}/R_s) \cdot \exp(-t/\tau_P)$

$I_R = V_C/R_m = V_{cmd}/(R_s+R_m)\, [1 - \exp(-t/\tau_P)]$

I_m change to voltage clamp (2)





Passive current response upon V_m change

$V_{cmd} = V_S + V_C$

$V_S = I_T R_S$

$V_C = (V_{cmd} R_m / R_T) \cdot [1 - \exp(-t/\tau_p)]$

$I_m = I_C + I_R$

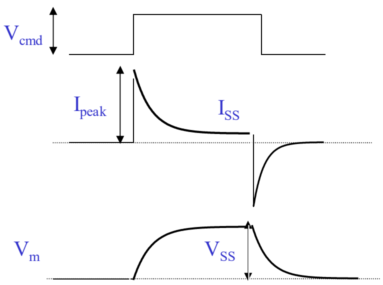
$I_C = (V_{cmd}/R_S) \cdot \exp(-t/\tau_p)$

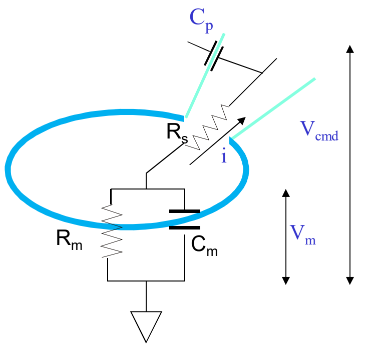
$I_R = (V_{cmd}/R_T)[1 - \exp(-t/\tau_p)]$,

$\tau_p \equiv R_p C_m$; $R_p \equiv R_m R_s / R_T$; $R_T \equiv R_m + R_s$.

$V_S = (V_{cmd}/R_T) \cdot (R_s + R_m \cdot \exp(-t/\tau_p))$

I_m change to voltage clamp (3)





$V_{ss} = V_{cmd} \cdot R_m / (R_m + R_s)$

$I_{peak} = V_{cmd} / R_s$

$I_{ss} = V_{cmd} / (R_m + R_s)$

$\tau_P \equiv R_P C_m \cong R_s C_m$,

Since $R_P \cong R_s$ (*if* $R_s << R_m$).

- $R_s = I_{peak} / V_{cmd}$.

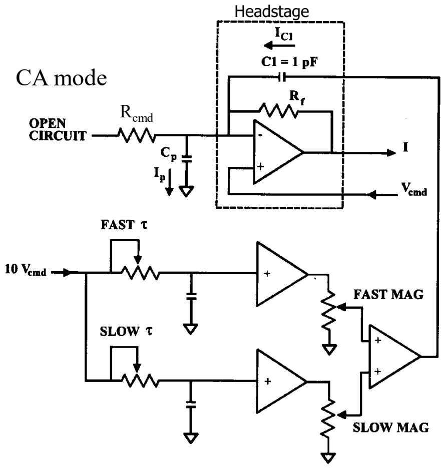
(I_{peak} *should be measured after complete* C_{fast} *cancellation*)

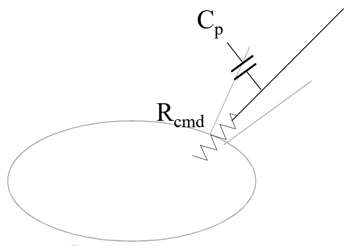
- $V_m = V_{cmd} - i R_s$.

(*The larger i causes the larger voltage drop at* R_s.)

- τ in CA mode ($= R_{cmd} C_p$) is faster than τ in WC mode ($= R_s C_m$)

Pipette capacitance cancellation (fast capacitance cancellation)





To compensate I_P,

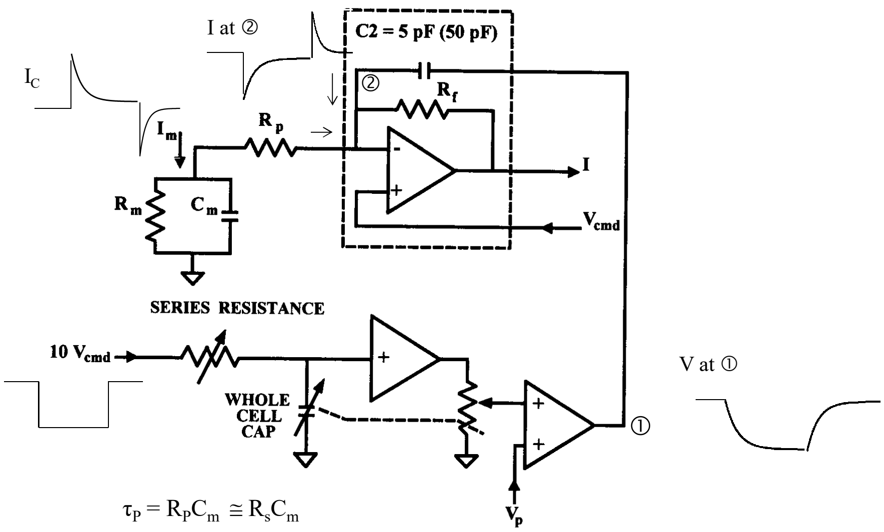
the CCC supplies a negative I_P (I_{C1})

to the input of headstage op amp

To make a negative I_P, V_{shaped} is made and supplied to C1

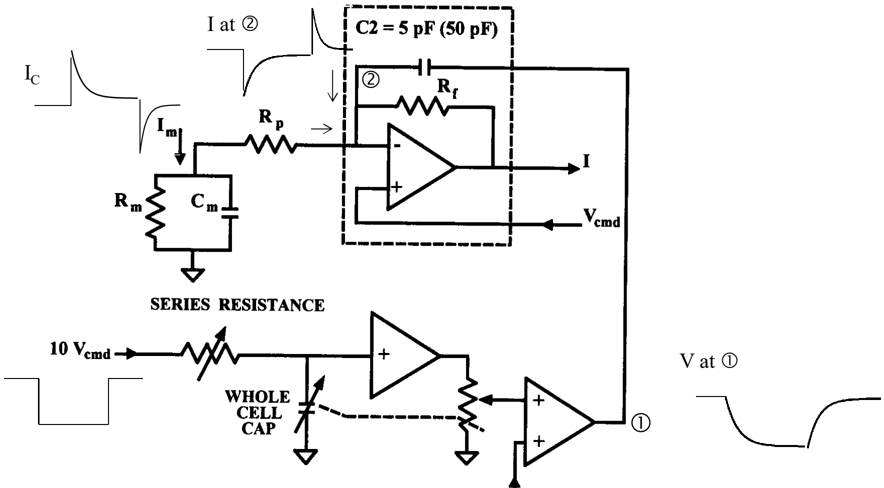
Cancellation of C_{fast} should be done prior to the estimation of R_S from I_{peak}/V_{cmd}.

Whole-cell capacitance cancellation



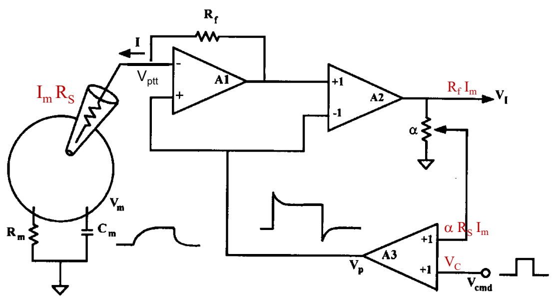
$\tau_P = R_P C_m \cong R_s C_m$

Whole-cell capacitance cancellation



$\tau_P = R_P C_m \cong R_s C_m$

Series resistance (R_S) compensation



$V_m = V_{ptt} - I_m R_S$,

Goal: $V_m = V_{cmd}$.

Mtd: $V_{ptt} \leftarrow V_{cmd} + \alpha I_m R_S$ $(0<\alpha<1)$

Rslt: $V_m = V_{cmd} - (1-\alpha) I_m R_S$

Overcompensation

When the current under observation has a positive feedback dynamics like I_{Na}, the R_s comp may cause a larger cell current leading to a positive feedback, especially when $\alpha \rightarrow 1$ and incomplete spatial clamp.

Once the circuit current is sat'd under such positive feedback conditions, the circuit starts to oscillate.

Off-line R_s compensation

Goal: Calc $G_m \Rightarrow I_{corr} = G_m V_{cmd}$.

I_T = measured current
I_R = I thr channels in cell mb
V_{cmd} = command potential

$I_T = I_R + I_C$ (I_R: I thr. R_m)

$$V_{cmd} = R_S I_T + V_m. \quad 1)$$

$$I_R = I_T - I_C = I_T - C_m dV_m/dt \quad 2)$$

When V_{cmd} = const, inserting 1) into 2) yields,

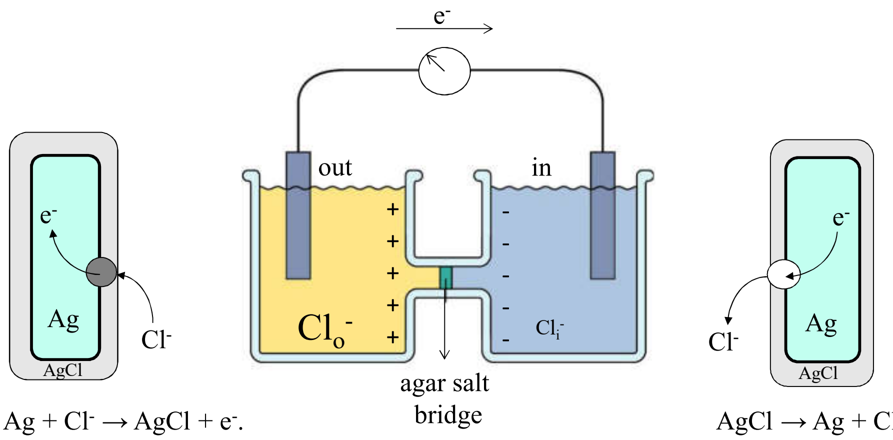
$$I_R = I_T + C_m R_s dI_T/dt$$

$$G_m = I_R / V_m = (I_T + C_m R_S dI_T/dt) / (V_{cmd} - R_S I_T).$$

$$I_{corr} = G_m V_{cmd} = V_{cmd} (I_T + C_m R_s dI_T/dt) / (V_{cmd} - R_S I_T)$$

Error sources

Liquid-Metal Junction Potential



$Ag + Cl^- \rightarrow AgCl + e^-$.

$AgCl \rightarrow Ag + Cl^-$.

$$V_i - V_o = -RT/F \ln[Cl_o/Cl_i]$$

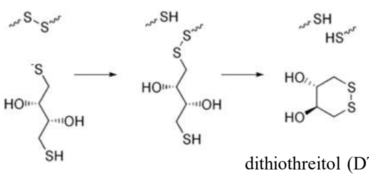
Redox artifacts

Methods In Cell Physiology

Am J Physiol Cell Physiol 304: C604–C613, 2013.
First published January 23, 2013; doi:10.1152/ajpcell.00318.2012.

Redox artifacts in electrophysiological recordings

Jonathan M. Berman and Mouhamed S. Awayda



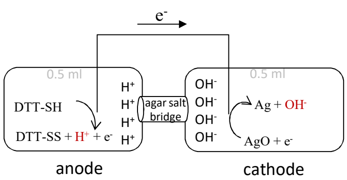
dithiothreitol (DTT)

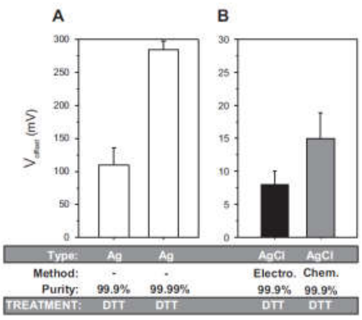
Bare silver electrode

cathode: $2AgO + 2e^- + 2H_2O \rightleftarrows 2Ag + 4OH^-$

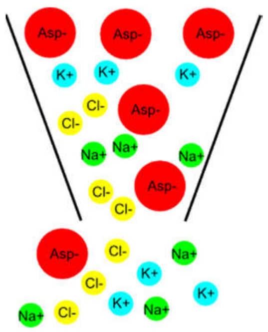
anode: $C_4H_{10}O_2S_2 \rightleftarrows C_4H_8O_2S_2 + 2H^+ + 2e^-$
(DTT)

$V_{offset} = V_{anode} - V_{cathode}$





Liquid Junction Potential (V_L)



Def. of V_L: the potential of bath with respect to the pipette sol.

$$V_L = (u\,E_{cation} - v\,E_{anion}) / (u + v),$$

where u (v): mobility of cation (anion)

$$E_{cation} = (RT/F)\ \ln\,[C_{cmd}/C_{bath}].$$

e.g)

145 K-Glutamate, +10 mV

145 KCl, +3 mV

145 Cs-Glutamate, +11 mV

$$V_m = V_i - V_{bath}.$$

Redox artifacts

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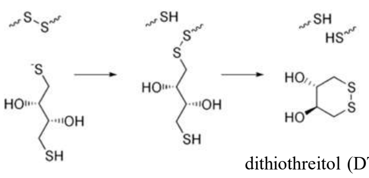

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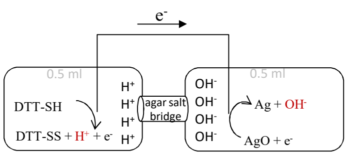
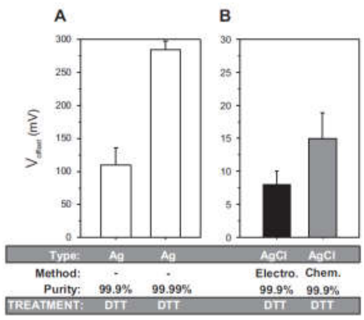
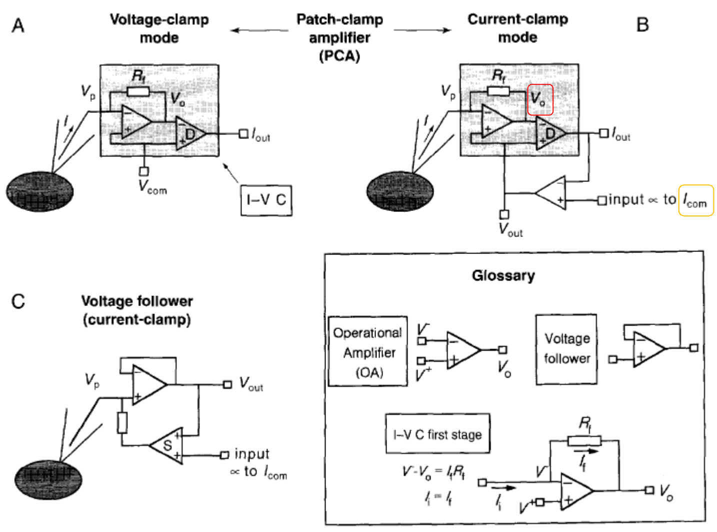
$V_{offset} = V_{anode} - V_{cathode}$

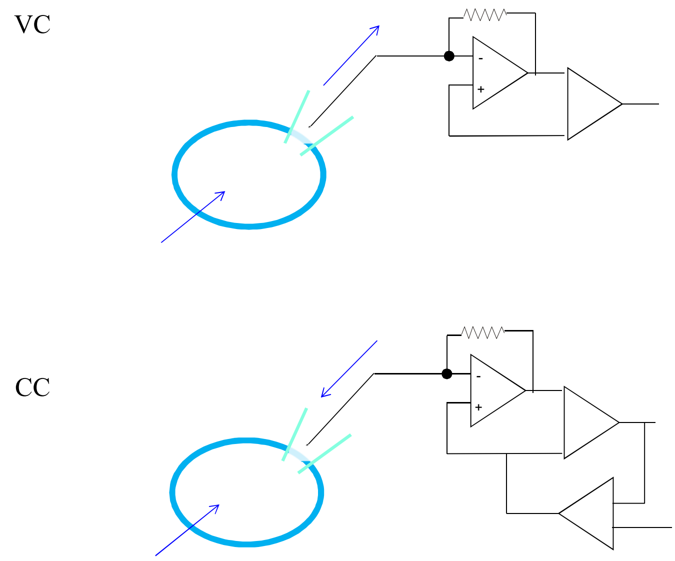




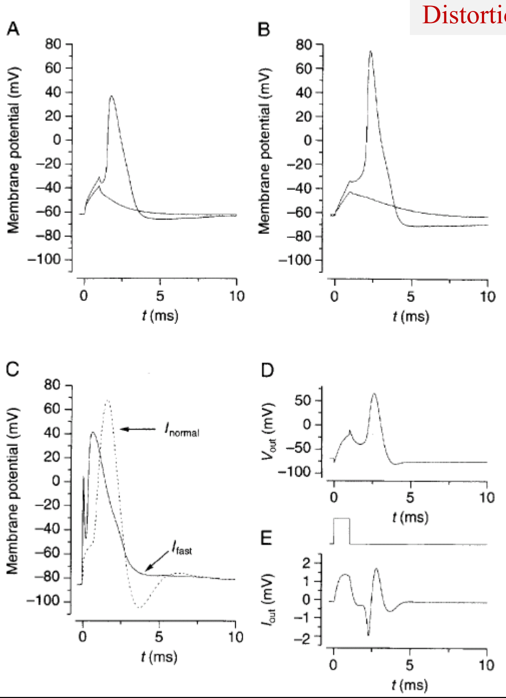
Action potentials recorded with patch-clamp amplifiers: are they genuine?



Magistretti Wanke (1996) TiNS



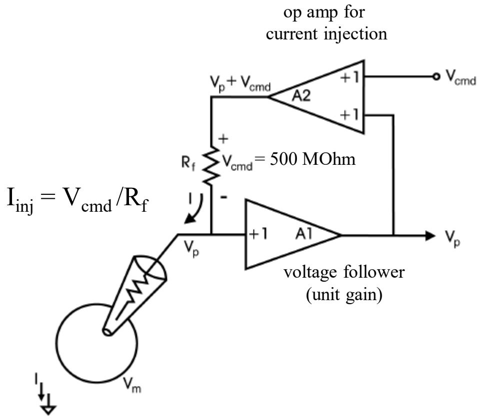
Distortion of AP recordings under CC mode



AP recordings of DRG neuron
A. bridge amp (Axoclamp 2A)
B. patch-clamp amp (Axopatch 1D)
C. Axopatch 200A
D-E. simultaneous recordings of Vm & Im using Axopatch 1D

Ideally, I_m should be zero under CC mode
Note that $I_m \neq 0$, because the amp rsp is not fast enough.

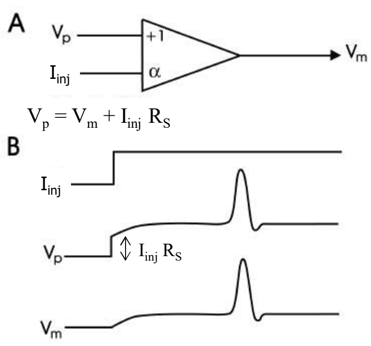
Now, head stages contain voltage follower as well as I-V converter circuit, since EPC10 and Multiclmap700B



Bridge Balance

Technique for separation of V_m from V_p

$V_p = V_m + I_{inj} R_S$



Dynamic clamp

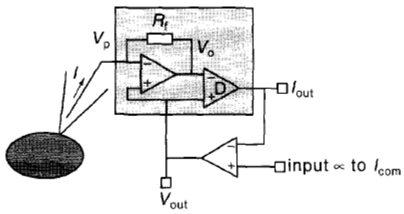
Monitoring V_m response under current clamp mode

caused by injection of current that follows

$I_{syn}(t) = g(t)\,[V_m(t) - E_{rev}]$.

1) E_{rev} and $g(t)$ are pre-specified
2) The injection current [$I_{syn}(t)$] should be constantly updated acc. to the equation with reference to instantaneously monitored V_m.

P25M high speed analog calculator



Filter

Euler's Formula

Taylor series of f(x) from x = 0

$$f(x) = f(0) + f'(0)x + \frac{f''(0)}{2!}x^2 + \frac{f^{(3)}(0)}{3!}x^3 + \ldots + \frac{f^{(n)}(0)}{n!}x^n + \ldots.$$

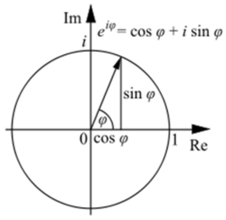
Proof of Euler's formula

$$e^{ix} = 1 + ix + \frac{(ix)^2}{2!} + \frac{(ix)^3}{3!} + \frac{(ix)^4}{4!} + \frac{(ix)^5}{5!} + \frac{(ix)^6}{6!} + \frac{(ix)^7}{7!} + \frac{(ix)^8}{8!} + \cdots$$

$$= 1 + ix - \frac{x^2}{2!} - \frac{ix^3}{3!} + \frac{x^4}{4!} + \frac{ix^5}{5!} - \frac{x^6}{6!} - \frac{ix^7}{7!} + \frac{x^8}{8!} + \cdots$$

$$= \left(1 - \frac{x^2}{2!} + \frac{x^4}{4!} - \frac{x^6}{6!} + \frac{x^8}{8!} - \cdots\right) + i\left(x - \frac{x^3}{3!} + \frac{x^5}{5!} - \frac{x^7}{7!} + \cdots\right)$$

$$= \cos x + i \sin x.$$



$\exp(j\theta) = \cos(\theta) + j\sin(\theta)$

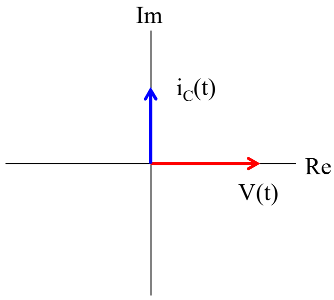
$\exp(-j\theta) = \cos(\theta) - j\sin(\theta)$

$A + j\,B = r\cdot\exp(j\theta)$,

where $r = \sqrt{|A^2 + B^2|}$,

$\theta = \arctan(B/A)$

Impedance of RC-Circuit



$v(t) = v_0 \cdot \cos(\omega t)$

$i_R(t) = [v_0/R] \cos(\omega t)$

$Z_R = R$

$i_C(t) = C\, dv/dt = -\omega C\, v_0 \sin(\omega t)$

$\exp(j\omega t) = \cos \omega t + j \sin \omega t$: Euler's formula

$v(t) = \mathrm{Re}[v_0 \exp(j\omega t)]$

$i_C(t) = C\, dv/dt = C \cdot \mathrm{Re}[v_0\, j\omega \exp(j\omega t)] = -\omega C\, v_0 \sin(\omega t)$

$Zc = 1/ j\omega C$

Fourier transform

A function on the time-domain, v(t), can be converted into another function on frequency domain, V(f), without loss of information

v(t) ⇔ V(f)

$$v(t) = \int_{-\infty}^{\infty} V(f)\cdot \exp(i\omega t)df \quad \Leftrightarrow \quad V(f) = \int_{-\infty}^{\infty} v(t)\cdot \exp(-i\omega t)dt$$

dv(t)/dt ⇔ jω $V(f)$

(derivatve theorem of Fourier transform)

Proof

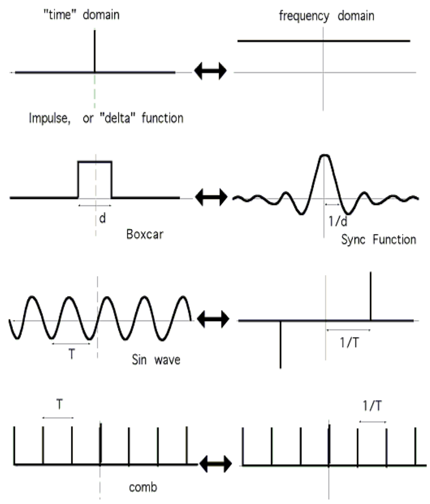
dV(f)/dt = ∫[dv/dt exp(-jwt) + v(t) (-jw) exp(-jwt)]dt

Since dV(f)/dt = 0

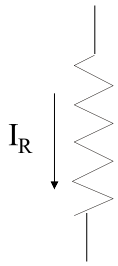
∫[dv/dt exp(-jwt)]dt = jw ∫[v(t) exp(-jwt)]dt = jw V(f)

$$\int_{-\infty}^{\infty} dv/dt \cdot \exp(-j\omega t)dt = jwV(f)$$

∴ dv(t)/dt ⇔ jω $V(f)$



Impedance of RC-Circuit



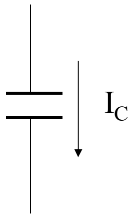
<u>Ohm's law</u>

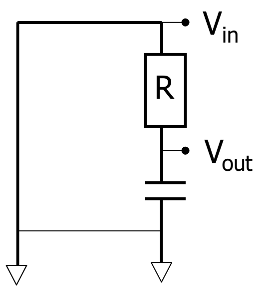
$I_R = V / R$
$Z_R = R$

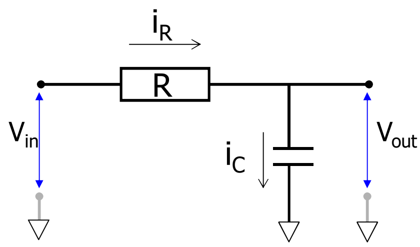
$Q = C \cdot V$
$dQ/dt = C \cdot dV/dt$
$i_C(t) = C \cdot dV/dt$

↓ F. T.

$I(f) = j\omega C\ V(f)$
$Z_c = j\omega C$







$i_R = i_C$,
$(V_{in} - V_{out}) / R = V_{out} / Z_c$.

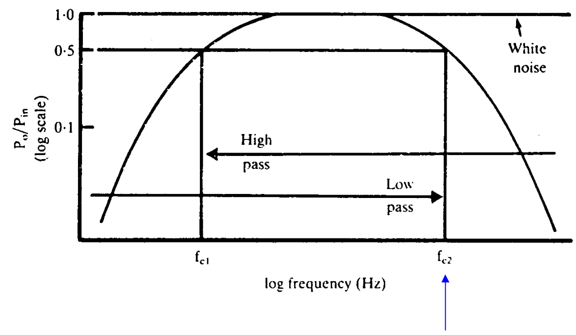
Since $Z_c = 1 / j\omega C$
$V_{out} = V_{in} / (1 + j\omega RC)$: *Transfer function*

<u>Rayleigh's Theorem</u>
$e(t) \Leftrightarrow E(f)$: F.T. pair
$\int |e(t)|^2\, dt = \int |E(f)|^2\, df$
: law of energy conservation

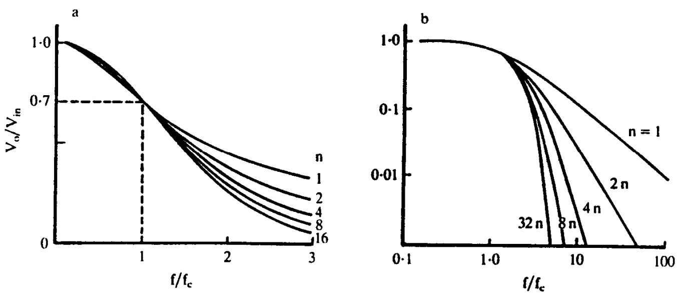
Power = $V \cdot V^*$
$V_{out} \cdot V_{out}^* = |V_{out}|^2 = |V_{in}|^2 / [1 + (\omega\tau)^2]$

Def. cut-off frequency $(f_c) \equiv f$ at $|V_{out}|^2 = |V_{in}|^2 / 2$
$(\omega_c \tau)^2 = (2\pi f_c \tau)^2 = 1$
$f_c = 1 / (2\pi\tau)$

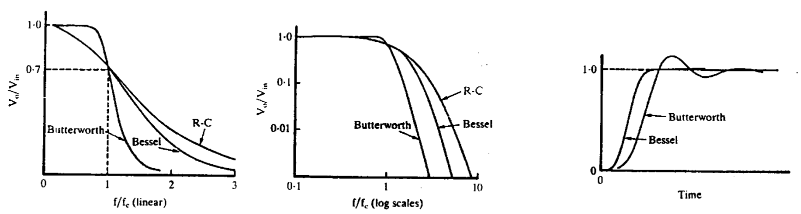
$|V_{in}|^2 = P_{in}$ —— **Filter** ——→ $|V_{out}|^2 = P_{out}$



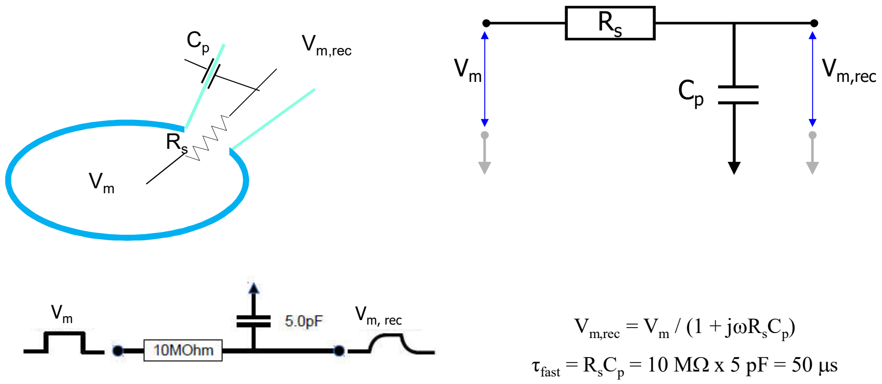
cut-off frequency
of low-pass filter



$V_{out} = V_{in} / (1 + (i2\pi f/f_c))$,



In CC mode, measured voltage is low-pass filtered version of real V_m



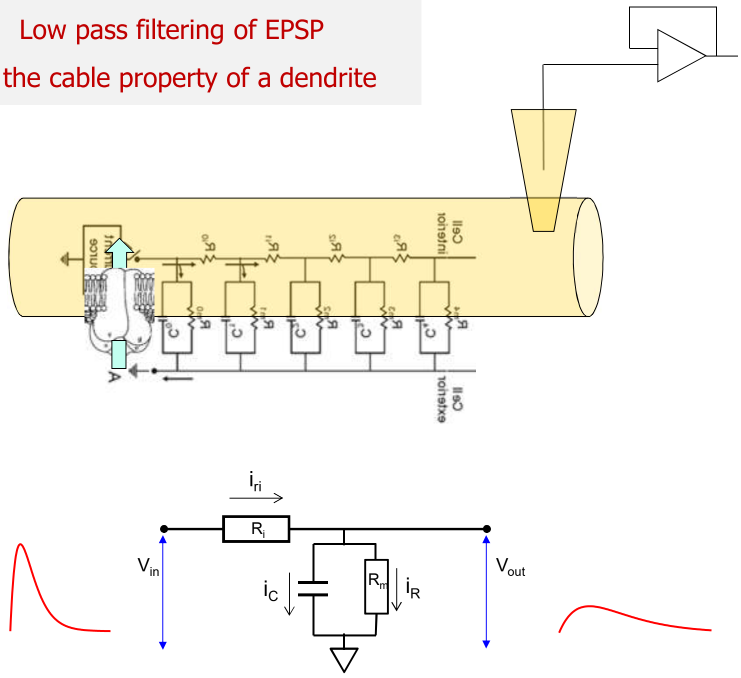
$$V_{m,rec} = V_m / (1 + j\omega R_s C_p)$$

$$\tau_{fast} = R_s C_p = 10\ M\Omega \times 5\ pF = 50\ \mu s$$

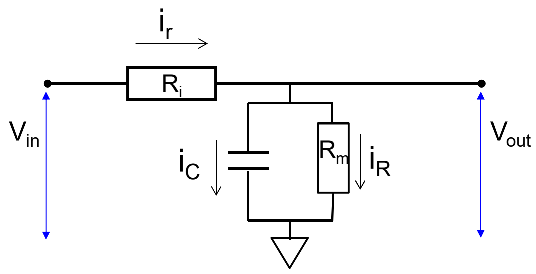
$$f_c = 1/(2\pi\ \tau_{fast}) = 3.2\ kHz$$

Low pass filtering of EPSP

by the cable property of a dendrite



Low-pass filtering of EPSP



$i_r = i_R + i_C$,

$(V_{in} - V_{out}) / R_i = V_{out} (1/Z_c + 1/R_m)$

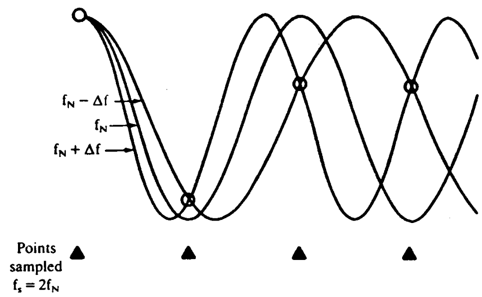
$V_{in} = V_{out} (R_i/Z_c + R_i/R_m + 1)$

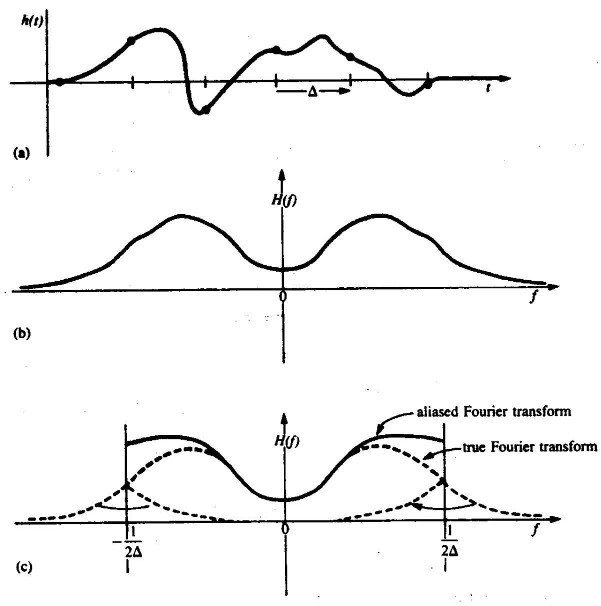
Since $Z_c = 1 / j\omega C$

$V_{out} = V_{in} / (1 + R_i/R_m + j\omega R_i C)$,

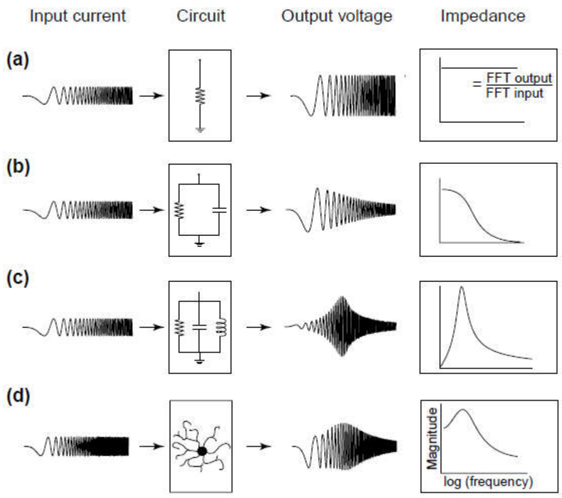
$V_{out} / V_{in} = 1 / (1 + R_i/R_m + j\omega R_i C) \cong 1 / (1 + j\omega R_i C)$

Aliasing – a digitization error

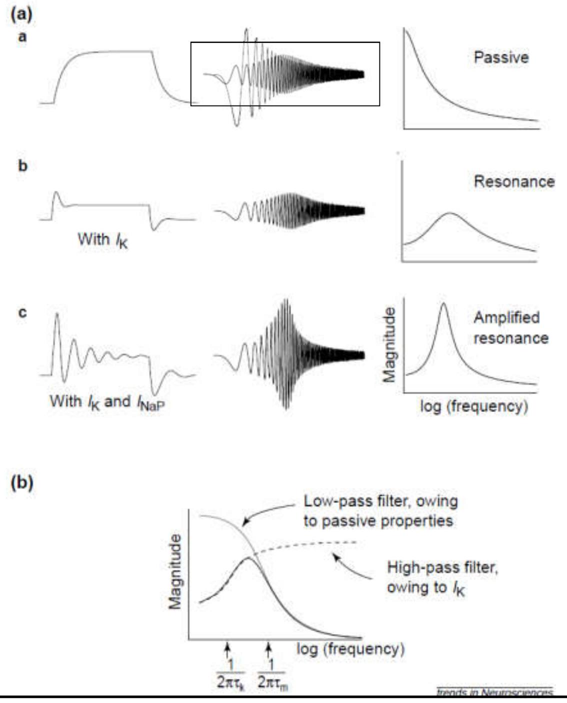




Resonance frequency in rsp to chirp stimulus current Tection



Hutcheon & Yarom (2010) TiNS



passive property only

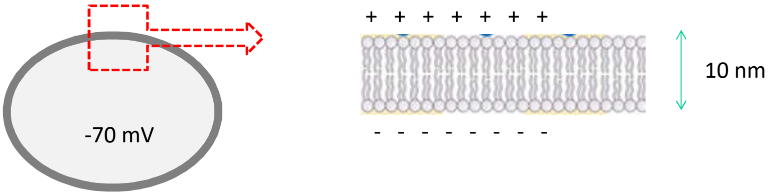
+ slowly activating conductance
(slower than τ of the cell)
(I_{kr} and/or I_h)

+ fast depolarizing current
that exerts positive feedback
to voltage change
($I_{Na,p}$ I_{NMDA} , $I_{Ca,L}$)

Cell Capacitance Monitoring

Cell membrane as a capacitor

0 mV

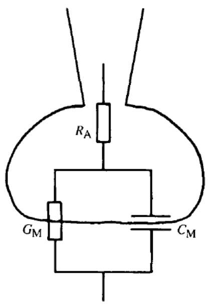


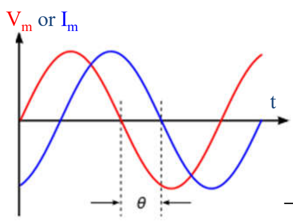
70 mV/ 10 nm = 7 MV/m

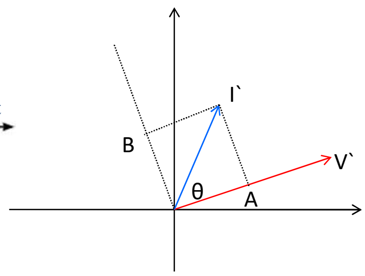
specific capacitance of lipid bilayer (ε) = 1 μF/cm^2.

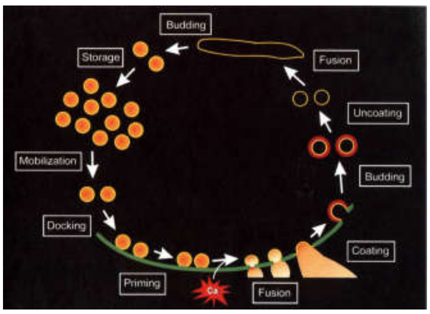
C_m = ε A, where A is the cell surface area

Capacitance Monitoring









Combined conductance

$Y(\omega) = (G_M + R_A (\omega C_M)^2 + j\omega C_M) / (1 + R_A^2 (\omega C_M)^2)$

$Re(Y) = [G_M + R_A (\omega C_M)^2] / [1 + R_A^2 (\omega C_M)^2]$

$Im(Y) = \omega C_M / (1 + R_A^2 (\omega C_M)^2)$

baseline phase shift = arctan(Im/Re)

$= \arctan [\omega C_M / (G_M + R_A (\omega C_M)^2)]$.

conductance (Y)
parallel combination: $Y = Y_1 + Y_2 + \ldots$
serial combination: $1/Y = 1/Y_1 + 1/Y_2 + \ldots$

impedance (Z)
parallel combination: $1/Z = 1/Z_1 + 1/Z_2 + \ldots$
serial combination: $Z = Z_1 + Z_2 + \ldots$

impedence of
resistor: R
capacitor: $1 / (j\omega C)$

conductance of
resistor: 1/R
capacitor: $j\omega C$

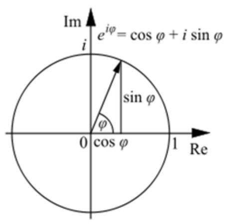
Euler's Formula

Taylor series of f(x) from x = 0

$$f(x) = f(0) + f'(0)x + \frac{f''(0)}{2!}x^2 + \frac{f^{(3)}(0)}{3!}x^3 + \ldots + \frac{f^{(n)}(0)}{n!}x^n + \ldots.$$

Proof of Euler's formula

$$e^{ix} = 1 + ix + \frac{(ix)^2}{2!} + \frac{(ix)^3}{3!} + \frac{(ix)^4}{4!} + \frac{(ix)^5}{5!} + \frac{(ix)^6}{6!} + \frac{(ix)^7}{7!} + \frac{(ix)^8}{8!} + \cdots$$
$$= 1 + ix - \frac{x^2}{2!} - \frac{ix^3}{3!} + \frac{x^4}{4!} + \frac{ix^5}{5!} - \frac{x^6}{6!} - \frac{ix^7}{7!} + \frac{x^8}{8!} + \cdots$$
$$= \left(1 - \frac{x^2}{2!} + \frac{x^4}{4!} - \frac{x^6}{6!} + \frac{x^8}{8!} - \cdots\right) + i\left(x - \frac{x^3}{3!} + \frac{x^5}{5!} - \frac{x^7}{7!} + \cdots\right)$$
$$= \cos x + i \sin x.$$



$\exp(j\theta) = \cos(\theta) + j\sin(\theta)$

$\exp(-j\theta) = \cos(\theta) - j\sin(\theta)$

$A + j\,B = r \cdot \exp(j\theta)$,

where $r = \sqrt{|A^2 + B^2|}$,

$\theta = \arctan(B/A)$

Phase shift

$v(t) = V' \cdot \exp(j\omega t)$

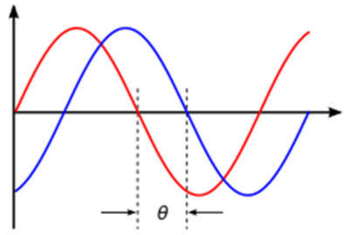
$i(t) = y(\omega) \cdot v(t) = I' \cdot \exp[j(\omega t + \theta)]$

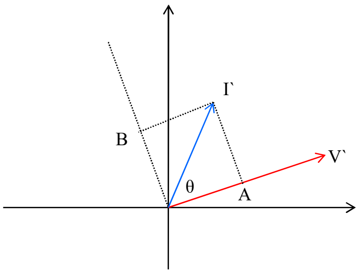
$y(\omega) = i(t)/v(t) = (I'/V') \cdot \exp(j\theta)$

$= (I'/V') \cdot (\cos\theta + j \sin\theta)$

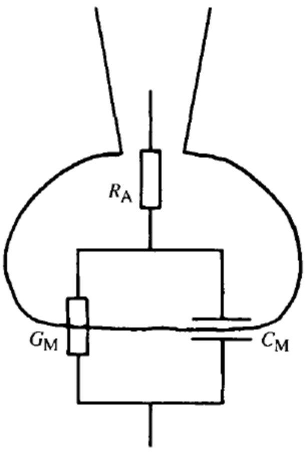
$= A + j B$

θ: phase shift = arctan(B/A)





Combined Conductance (Y)



$Y_M = G_M + j\omega C_M.$

$Y_A = 1/R_A.$

$1/Y = 1/Y_M + 1/Y_A.$

$$\frac{1}{Y(\omega)} = \frac{1}{(G_M + j\omega C_M)} + R_A$$

$$Y(\omega) = \frac{G_M + j\omega C_M}{1 + R_A G_M + R_A (j\omega C_M)}$$

When $G_M << 1/R_A$,

$Y(\omega) = (G_M + R_A (\omega C_M)^2 + j\omega C_M) / (1 + R_A^2 (\omega C_M)^2)$

$Y(\omega) = (G_M + j\omega C_M) / (1 + R_A G_M + R_A (j\omega C_M))$

$Y(\omega) = (G_M + R_A (\omega C_M)^2 + j\omega C_M) /(1 + R_A^2 (\omega C_M)^2)$

$Re(Y) = [G_M + R_A (\omega C_M)^2] / [1 + R_A^2 (\omega C_M)^2]$

$Im(Y) = \omega C_M / (1 + R_A^2 (\omega C_M)^2)$

baseline phase shift = arctan(Im/Re)

= $\arctan [\omega C_M / (G_M + R_A (\omega C_M)^2)]$.

$Y(\omega) = [G_M + R_A (\omega C_M)^2 + j\omega C_M] / [1 + R_A^2 (\omega C_M)^2]$

e.g.)

Let $C_m = 5$ pF, $R_a = 10$ MΩ, $R_m = 2$ GΩ, f = 1 KHz

baseline phase shift ?

baseline phase shift (q) = $\arctan \{\omega C_M / [G_M + R_A (\omega C_M)^2]\} = 71.74$

Lindau-Neher Technqiue

$$Y(\omega) = [G_M + R_A (\omega C_M)^2 + j\omega C_M] / [1 + R_A^2 (\omega C_M)^2]$$

$Y(\omega) = A + j\,B$

$A = [G_M + R_A (\omega C_M)^2] / [1 + R_A^2 (\omega C_M)^2]$

$B = \omega C_M / [1 + R_A^2 (\omega C_M)^2]$

$I_{dc} = (V_{dc} - E_r)\cdot G_t$, where $G_t = 1/(R_M + R_A)$.

$$C_m = \frac{1}{\omega_c B}\frac{(A^2 + B^2 - AG_t)^2}{(A - G_t)^2 + B^2} \qquad R_m = \frac{1}{G_t}\frac{(A - G_t)^2 + B^2}{A^2 + B^2 - A\,G_t}$$

Extracellular Recording of Neural Acitivity

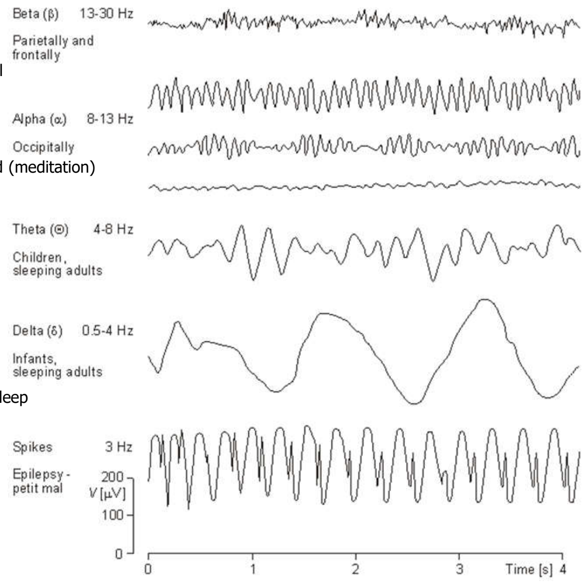
Electroencephalogram (EEG)

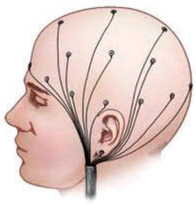
arousal

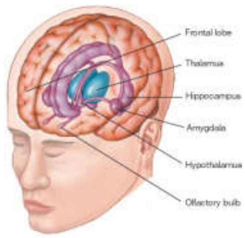
relaxed (meditation)

sleep

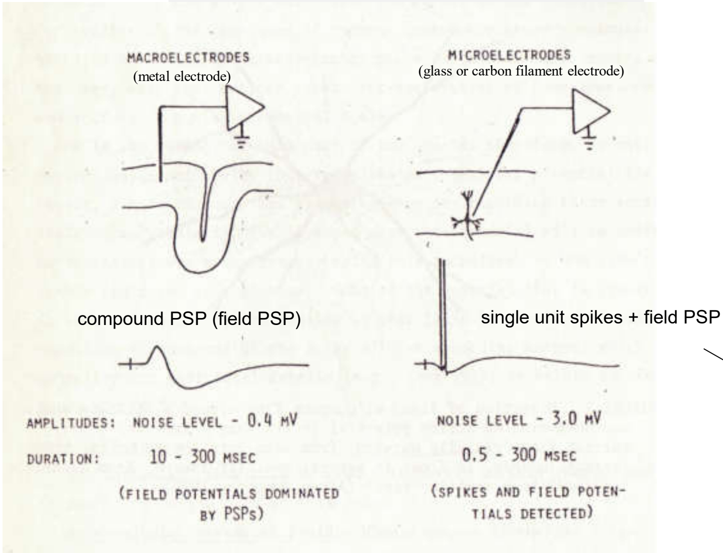
deep sleep

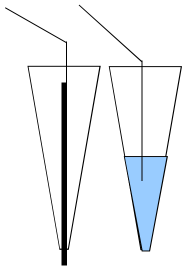






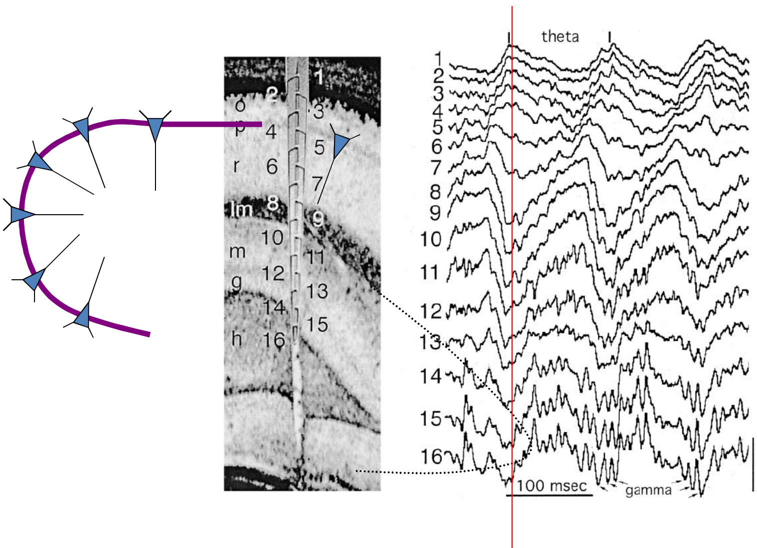
Macro- vs Micro-electrode





dimension of the exposed tip of a microelelctrode:
< 5 µm in diameter and < 20 µm in length

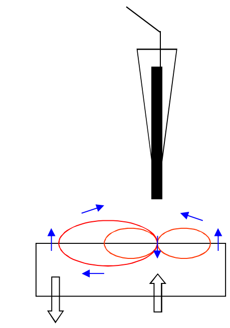
Pyramidal neuron as a current dipole

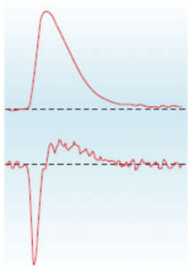


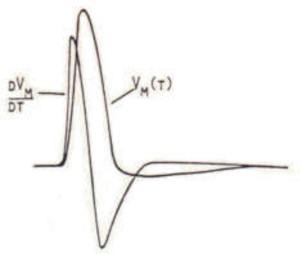
The gradual phase reversal: supports the theory of a pyr cell as a dipole

hippocampal field potential rec'd by macroelectode

Extracellular recording of single unit action potential







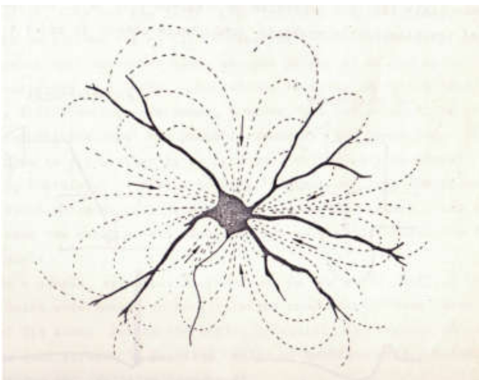
*Good extracellular recording electrode

- small: unit spike activity
- low impedance: high S/N ratio

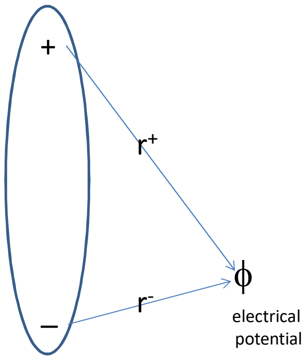
carbon filament and platinum black

Field potential

a potential difference generated by a flow of current thr. finite extracelluar (EC) medium



Direction lines of EC current flow around a stellate cell during somtic action potential



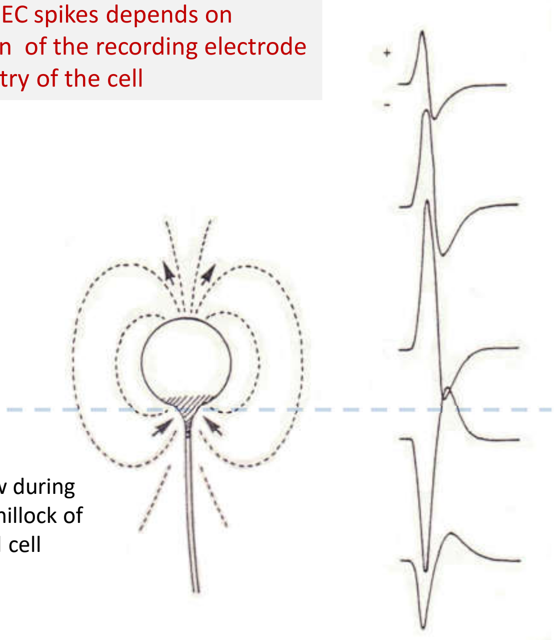
$$\varphi = \frac{1}{4\pi\sigma}\left(\frac{J^+}{r^+} - \frac{J^-}{r^-}\right)$$

When $J^+ = J^-$,

$$\varphi = \frac{J}{4\pi\sigma}\left(\frac{1}{r^+} - \frac{1}{r^-}\right)$$

J, charge
r, distance
σ, bulk conductivity

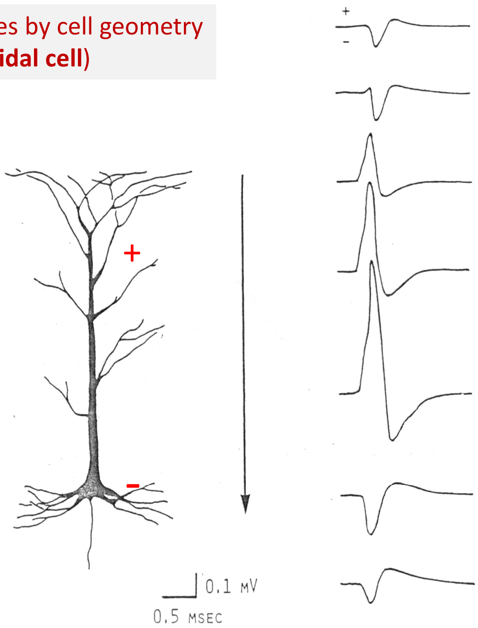
The shape of EC spikes depends on
1) the location of the recording electrode
2) the geometry of the cell



EC current flow during an AP at axon hillock of a spherical cell

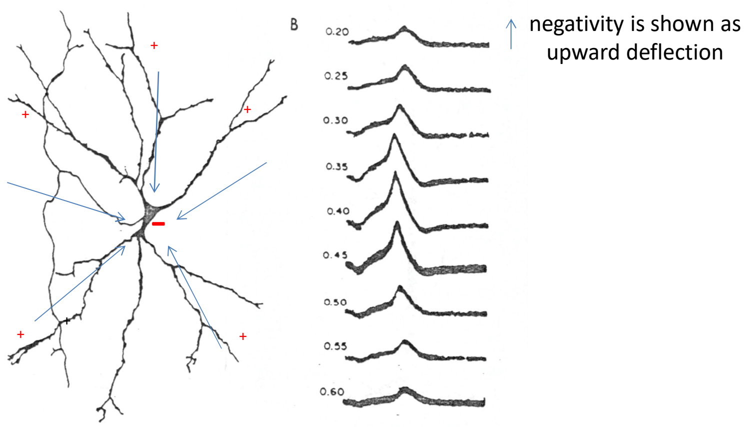
EC spikes recorded from electrodes at different depth

Shaping of EC spikes by cell geometry (**pryamidal cell**)



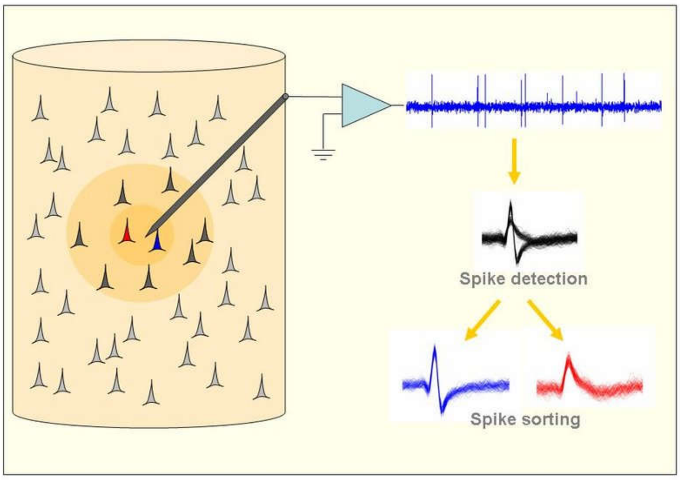
EC spikes at different electrode locations during an somatic APdu

Shaping of EC spikes by cell geometry (**stellate cell**)

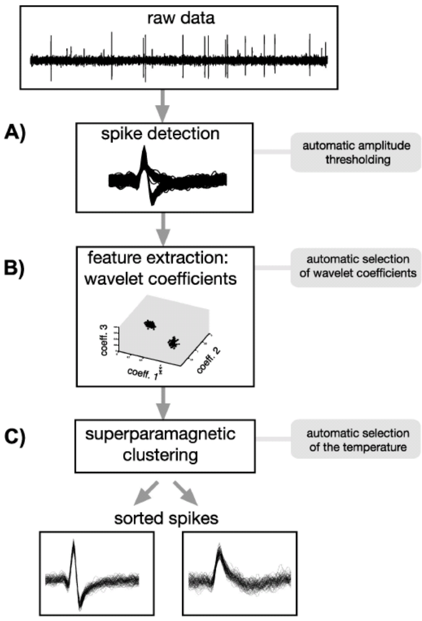


Dendtric current sources (J^+) are more distributed in SC than in PC
⇒ Concentrated sink at the soma dominates the EC spike everywhere.

Spike sorting



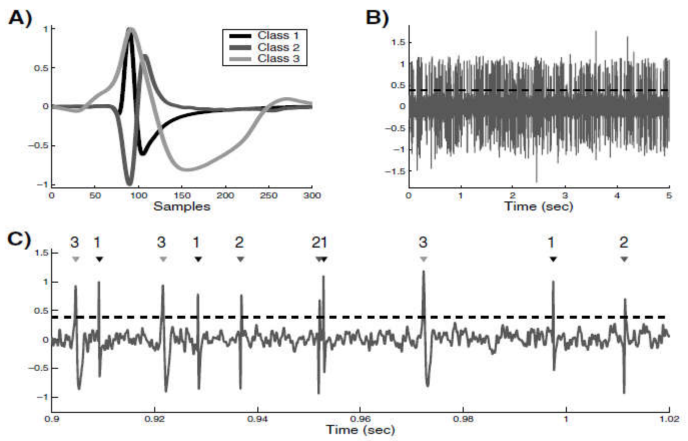
unbiased spike sorting



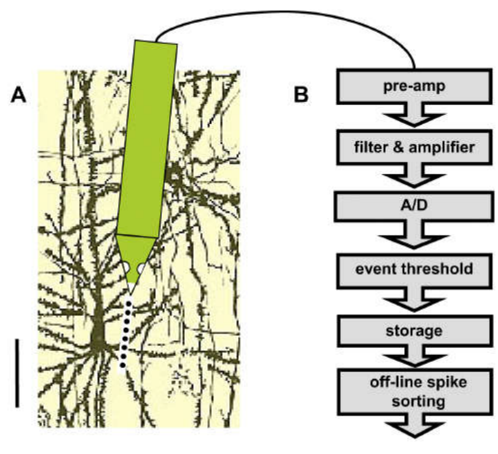
setting an amplitude threshold

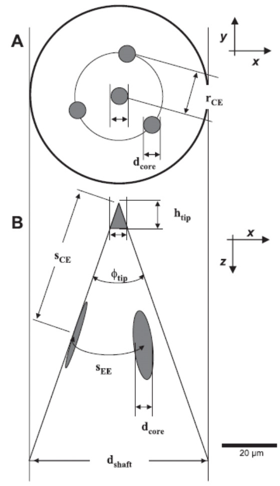
a set of wavelet coefficients

= relevant features for a group of spikes



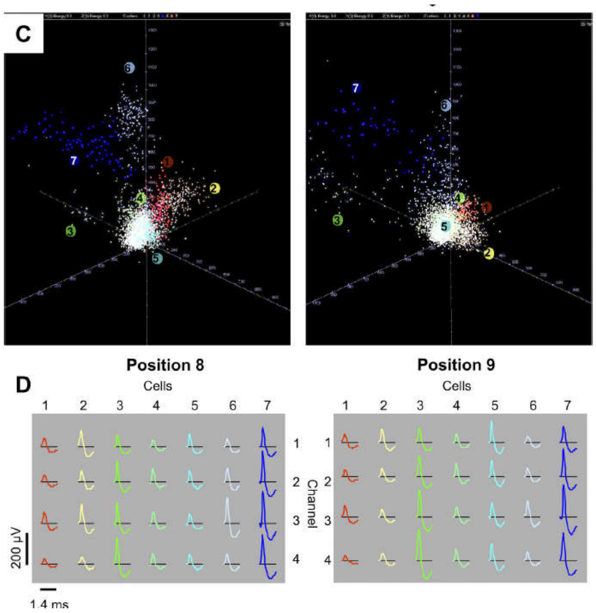
Tetrode





Mechler et al. (2011) J Neurophysiol 106: 828-848

Energy of waveforms recorded three channels of a tetrode at two different consecutive steps.



Mean spike waveforms on 4 channels (row) for each single units (col) identified in 2 steps of C